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Saccades Differentially Modulate Human LGN and V1 Responses in the Presence and Absence of Visual Stimulation

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Summary

Saccades occur several times each second in normal human vision. The visual image moves across the retina at high velocity during a saccade, yet no blurring of the visual scene is perceived [1, 2, 3, 4, 5]. Active suppression of visual input may account for this perceptual continuity, but the neural mechanisms underlying such saccadic suppression remain unclear. We used functional MRI to specifically examine responses in the lateral geniculate nucleus (LGN) and primary visual cortex (V1) during saccades. Activity in both V1 and LGN was strongly modulated by saccades. Furthermore, this modulation depended on whether visual stimulation was present or absent. In complete darkness, saccades led to reliable signal increases in V1 and LGN, whereas in the presence of visual stimulation, saccades led to suppression of visually evoked responses. These findings represent unequivocal evidence for saccadic suppression in human LGN and retinotopically defined V1 and are consistent with the earliest site of saccadic suppression lying at or before V1.

Results

The precise nature and location of saccadic influences on the human visual system are not clear. Indirect evidence suggests that the earliest stages of human visual processing are suppressed peri-saccadically. Psychophysically, saccadic suppression occurs beyond the retina [3], but prior to the site of contrast masking [4], and precedes visual motion analysis [6]. Visual phosphenes generated by transcranial magnetic stimulation (TMS) of human occipital cortex are perceived during saccades, whereas those produced by electrical stimulation of the eye are suppressed [7]. This suggests that saccades modulate visual processing at or before primary visual cortex (V1). Consistent with this, single-cell responses in monkey V1 and lateral geniculate nucleus (LGN) show substantial changes in activity during saccades [8, 9, 10]. In humans, although saccadic suppression has been observed in higher visual areas [11], and regions of occipital visual cortex show modulation of responses during saccades [12, 13, 14, 15], there has been no direct examination of activity in either retinotopically defined V1 or LGN during saccades.

In addition to uncertainty over the loci involved in saccadic suppression, empirical findings have not produced a consistent view of the nature of the modulatory influence of saccades on visual processing. In monkeys, saccades cause both enhancement and suppression of single-neuron responses in LGN, V1, middle temporal area (MT), and middle superior temporal area (MST) compared to fixation [8, 9, 10, 16]. In humans, both positive [12, 15] and negative [13, 14] saccade-related signals have been observed in occipital cortex. One possible reason for these discrepant findings could be that the effect of saccades on visual cortex may depend on the precise conditions of visual stimulation. For example, for saccadic suppression to be observed, visually responsive neurons might need to exhibit a minimum level of tonic activity.

To address these questions, we measured activity in LGN and V1 using functional magnetic resonance imaging (fMRI) while subjects made saccades under different visual conditions. We independently manipulated the presence (versus absence) of saccades, the presence (versus absence) of full-field flickering visual stimulation, and the nature of the visual flicker (isoluminant or achromatic). Participants wore diffuser goggles to ensure that eye movements did not alter the spatiotemporal structure of the retinal image (see Experimental Procedures). We performed two analyses of the fMRI data: a whole brain analysis to confirm activation of cortical oculomotor control regions (see the Supplemental Data available with this article online) and individual retinotopic analyses to examine any modulatory effects of saccades on early visual areas.

Primary Visual Cortex and LGN

Activity in V1 and LGN was similarly altered by saccades in both areas. Saccades strongly affected Blood Oxygenation Level-Dependent (BOLD) responses both in the presence and absence of visual stimulation but in opposite directions (Figures 1A and 1B). In darkness, there was a significant increase in activity during saccades compared to the no-saccade condition in V1 and LGN. During visual stimulation, there was a significant decrease in activity for chromatic and achromatic visual stimuli during saccades compared to the no-saccade condition in both V1 and LGN, with no significant interaction between eye movements and type of visual stimulus (chromatic/achromatic) in either area. Individual subjects follow the trend that was shown in the group analysis (see Supplemental Data). Formal quantification of the degree of saccadic suppression during visual stimulation revealed greater suppression in LGN compared to V1 (Figure 1C).

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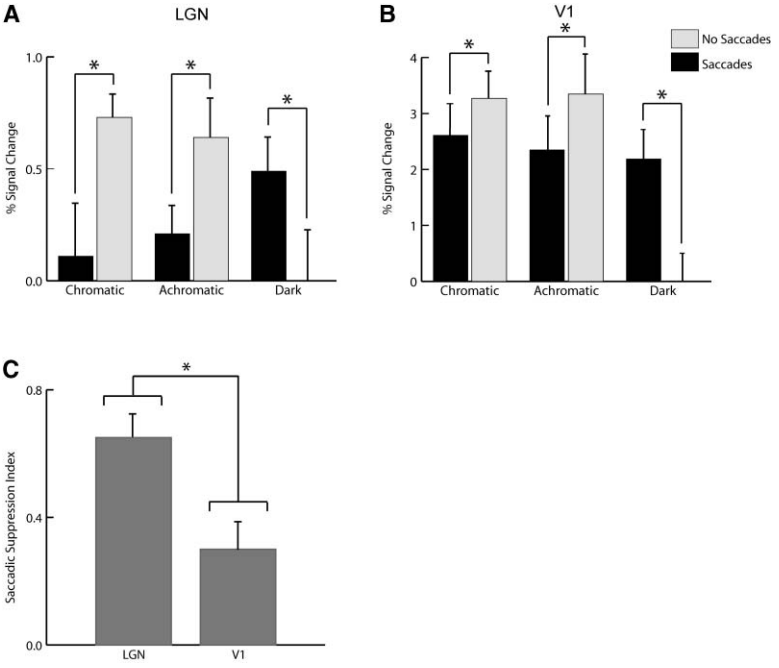

Figure 1. Modulation of Responses in Human LGN and V1 by Saccades

(A and B) BOLD contrast responses in human LGN (A) and V1 (B) during saccade and no saccade conditions in darkness and in the presence of chromatic or achromatic visual stimulation. Data are taken from individual subject retinotopic analyses (see Experimental Procedures). The percent-signal change is plotted as a function of condition and averaged across seven subjects (see Experimental Procedures; error bars ± 1 SE). Saccade conditions are plotted in black and no-saccade conditions are plotted in light gray. Both LGN and V1 show significantly increased BOLD signal during saccades in darkness compared to no saccades in darkness (LGN ($t(6) = 4.3$, $p = 0.005$, and V1 ($t(6) = 5.32$, $p = 0.002$) but significantly decreased signal for chromatic and achromatic stimuli during saccades compared to the same stimuli during no saccade conditions (LGN chromatic: $t(6) = -2.6$, $p = 0.047$, achromatic: $t(6) = -3.3$, $p = 0.017$; and V1 chromatic: $t(6) = -3.2$, $p = 0.019$, achromatic: $t(6) = -4.9$, $p = 0.003$). There was no significant interaction between eye movements and the type of visual stimulus (chromatic/achromatic) in V1 ($F(1,6) = 3.006$, $p = 0.134$) or LGN ($F(1,6) = 1.54$, $p = 0.26$).

(C) Saccadic effects were quantified and normalized to give an index of modulation of responses to visual stimulation in LGN and V1. Index values were computed for each subject based on the mean responses obtained in the saccade and no saccade conditions for each type of visual stimulus. Averaged index values are presented for seven subjects (see Experimental Procedures, error bars ± 1 SE). Larger values represent greater suppression of responses during saccadic eye movements. Suppression effects were greater for LGN than V1 ($t(6) = -4.02$, $p = 0.007$). The asterisk (*) denotes statistical significance ($p < 0.05$, two-tailed).

Higher Visual Areas

Higher visual areas V2, V3, and V5/MT showed a qualitatively similar pattern of modulation to LGN/V1, but responses were weaker overall (Figure 2). Saccades in darkness resulted in significant increases in activity in V2 and a trend toward significance in V3. Responses of V5/MT were not affected by saccades in darkness, but responses overall were weak, suggesting that the visual stimuli used were not optimal for activating V5/MT. During visual stimulation, saccades evoked small reductions in activity that did not reach significance in V2, V3, and V5/MT. This pattern of results did not differ between dorsal and ventral portions of V2/V3.

Discussion

Saccades altered activity in LGN and retinotopic visual cortex in two distinct ways. First, the presence (versus absence) of saccades was associated with significant modulation of activity in both the LGN and V1. Second, this modulation differed depending on whether saccades were made in the presence or absence of visual stimulation.

LGN and V1 Activity Is Modulated during Saccades

A recent TMS study suggested that saccadic suppression occurs at or before V1 [7]. However, this study could neither unequivocally identify V1 as the site of modulation nor examine the influence of saccades on subcortical structures. In contrast, our findings represent the first unambiguous evidence for saccadic modulation of activity in retinotopically-defined V1 and confirm that modulatory signals associated with saccades can also be seen in the human LGN. In monkey LGN, both facilitation or weak suppression followed by stronger facilitation of visual responses are seen in single trials, with suppression of burst firing over longer time intervals [8, 9]. The precise relationship between these multiphasic responses and BOLD contrast fMRI signals remains to be determined [17], but our observations show that the overall fMRI signal in human LGN to visual stimulation is suppressed during saccades.

Functional MRI is sensitive to both feed-forward and feedback signals [17]. Our findings of LGN modulation by saccades are therefore consistent either with a direct effect of oculomotor signals on the LGN or an indirect effect of feedback signals from V1. However, the relative degree of saccadic suppression of responses to visual stimulation was greater for LGN than for V1 (Figure 1C). One possibility is that this may relate to methodological differences in recording fMRI signals from cortical and subcortical structures. However, fMRI measurement of LGN and V1 contrast response functions reveal similar monotonic increases in BOLD activation with increasing stimulus contrast [18]. An alternate possibility is that feedback from V1 is not the only source of the LGN modulation that we observed. The LGN is well placed to receive direct modulatory influences from the oculomotor system due to its connections with the superior colliculus, a crucial structure in saccade generation [19]. Intriguingly, greater modulation of LGN (versus V1) responses is also seen during voluntary shifts of spatial attention [20]. It has been proposed that this arises from direct top-down influences of attentional signals on LGN

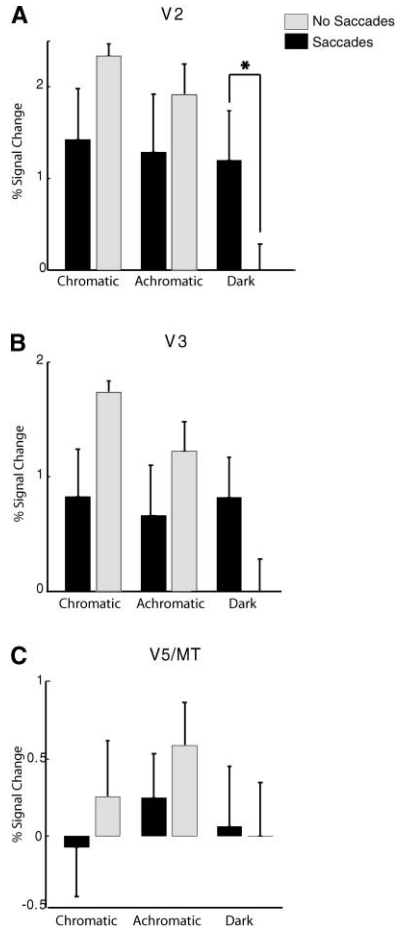

Figure 2. Modulation of Responses in Human V2, V3, and V5/MT by Saccades

BOLD contrast responses in human V2 (A), V3 (B), and V5/MT (C) during saccade and no-saccade conditions in darkness and in the presence of chromatic or achromatic visual stimulation. Data are taken from individual subject retinotopic analyses (see Experimental Procedures). The percent-signal change is plotted as a function of condition and averaged across seven subjects (error bars $\pm$ 1 SE). Saccade conditions are plotted in black and no-saccade conditions in light gray. Both V2 (A) and V3 (B) show increased BOLD signal during saccades in darkness compared to no saccades in darkness (V2, $t(6) = 2.52$, $p = 0.045$, V3 ($t(6) = 2.3$, $p = 0.061$). V5/MT (C) shows no modulation of responses during saccades in darkness ($t(6) = 0.19$, $p = 0.85$). Responses to chromatic and achromatic stimuli during saccades compared to the same stimuli during no saccade conditions were reduced, but not significantly in V2 (chromatic: $t(6) = -1.99$, $p = 0.09$, achromatic: $t(6) = -1.44$, $p = 0.2$), V3 (chromatic: $t(6) = -2.2$, $p = 0.07$, achromatic: $t(6) = -1.59$, $p = 0.16$), and V5/MT (chromatic: $t(6) = -0.9$, $p = 0.39$, achromatic: $t(6) = -1.5$, $p = 0.17$). There was no significant interaction between eye movements and visual stimulus type (V2: $F(1,6) = 0.85$, $p = 0.39$, V3: $F(1,6) = 1.38$, $p = 0.29$, V5/MT: $F(1,6) = 0.09$, $p < 0.7$). The asterisk (*) denotes statistical significance ($p < 0.05$, two-tailed).

rather than feedback from V1 [20]. Our findings suggest that LGN activity can be influenced not only by attentional but also by extra-retinal oculomotor signals.

Saccadic Suppression Depends on Visual Stimulation

Saccadic effects on LGN and retinotopic visual cortex differed in the presence and absence of visual stimulation. In darkness, saccades evoked a positive BOLD signal in LGN, V1 (Figure 1), and to a lesser degree higher retinotopic areas (Figure 2). However, during visual stimulation, saccades reduced the signal in both LGN and V1. This differential modulation of activity cannot be accounted for by changes in saccade rate, which was the same in all conditions. Instead, the saccadic modulation of activity in LGN and V1 that we observed may reflect the superposition of a positive signal (corollary discharge) that is independent of visual stimulation and a negative signal (saccadic suppression) that is dependent on the presence of visual stimulation. This is consistent with a proposed theoretical model of saccadic suppression based on psychophysical data [3]. The existence of two distinct modulatory effects of saccades on early visual areas may go some way in explaining the previously disparate neuroimaging findings regarding saccadic suppression, which took place under different conditions of visual stimulation. For example, Kleiser and colleagues [11] found suppression under conditions of visual stimulation, whereas Bodis-Wollner and colleagues [13, 14] found enhancement in darkness, consistent with the present findings (however, see [15]). To examine this issue further, future studies of saccadic influences in early visual areas should systematically vary the presence of visual stimulation under which saccades take place in order separate the influence of corollary discharge and saccadic suppression.

We did not psychophysically measure perceptual suppression during saccades, so any connection between perception and brain activity must be tentative. Psychophysically, perception of achromatic visual stimuli is suppressed more strongly than for chromatic stimuli [4] even for uniform full-field stimuli such as ours [21]. However, we did not find any evidence for selective suppression of achromatic stimuli during saccades in LGN and early visual cortex. Rather, we found that saccades significantly modulated the processing of both achromatic and chromatic stimuli in these areas. It is possible that the "low" spatial frequency of our full-field flicker stimulus did not optimally drive the parvocellular system in early visual cortex. It should also be noted that equiluminance is very difficult to achieve over large fields as it varies with eccentricity, so the stimuli we used may not be perfectly isoluminant over their full spatial extent. Despite these caveats, our findings are consistent with recent observations that selective suppression of magnocellular processing during saccades can be observed in higher visual areas such as V5/MT rather than in early visual cortex [11].

Taken together, these findings may argue against the notion of saccadic suppression as a unitary process resulting from modulation of activity at a single cortical location. Instead, it may manifest itself in different ways depending on the nature of the visual stimulus, consistent with the idea that the perceptual phenomenon of saccadic suppression results from an interaction of oculomotor and visual signals [3].

Experimental Procedures

Ten healthy subjects gave written informed consent to participate in the study (approved by the local ethics committee). Following scanning, three subjects were rejected on the basis of excessive

head movement (>5 mm). Seven subjects (all male, mean age 30 years) were included in the analyses reported here.

Subjects lay supine in the scanner, wearing customized spherical goggles made of semiopaque plastic that created near-Ganzfeld conditions (see Supplemental Data). While wearing the goggles, subjects reported seeing uniform black in the dark condition. During visual stimulation, subjects could identify whether the stimulus was chromatic or achromatic but perceived the visual stimulus as uniform throughout the visual field. This provided a featureless visual stimulus that lacked distinctive saccadic targets and was free from perceived contours that might move across the retina during saccades.

Visual stimuli were projected from an LCD projector (NEC LT158, refresh rate 60 Hz) onto the surface of the goggles via a mirror positioned within the head coil. All stimuli were presented using MATLAB (Mathworks Inc.) and COGENT 2000 toolbox (www.vislab.ucl.ac.uk/ cogent/index.html). Visual stimuli consisted of full-field flicker of either achromatic (black/white) or chromatic (isoluminant red/green) stimuli (time-averaged luminance: 9.5 Cd/m^2) at a rate of 7.5 Hz (eight screen refresh cycles) presented for 30 s. Isoluminance of the chromatic flicker stimulus was established for each individual subject by using flicker photometry (see Supplemental Data).

In the main experiment, two factors were manipulated independently in a 2×3 factorial blocked design. The factors were saccades (present or absent) and visual stimulation (chromatic flicker, achromatic flicker, or no flicker), giving a total of six conditions. During scanning, conditions were presented pseudorandomly in blocks of 30 s with a 20 s rest period between blocks (rest periods were not modeled in the subsequent analysis). Each block was preceded by an auditory command presented through pneumatic headphones that instructed subjects to either move their eyes or keep their eyes still. A sequence of pacing tones at 1.5 Hz was presented auditorily throughout each block. In "saccade" blocks, subjects were instructed to make a large horizontal saccade with their eyes open in response to each tone. In "no-saccade" blocks, subjects were instructed to fixate centrally with their eyes open. Electrooculographic (EOG) recording in three participants confirmed that they were able to reliably make paced horizontal saccades at 1.5 Hz during each saccade block and made no more than one saccade in total in each no-saccade block. Saccade amplitude for two subjects under simulated experimental conditions was 35° either side of central fixation (SD $\pm$ 5°) and was not significantly different across visual stimulation conditions.

Imaging and Analysis

A 3T Siemens Allegra system was used to acquire BOLD contrast image volumes. Volumes were acquired continuously every 2.6 s, each comprising 40 contiguous 3-mm-thick slices, giving whole brain coverage with an in-plane resolution of 3×3 mm. Six scanning runs of 110 image volumes were then acquired (one subject completed only four runs due to technical difficulties).

Imaging data were analyzed using SPM2 (www.fil.ion.ucl.ac.uk/spm). After discarding the first five image volumes from each run to allow for T1 equilibration effects, image volumes were realigned, coregistered to each subject's structural scan and smoothed with an isotropic 6mm Gaussian kernel [22]. Activated voxels in each experimental condition were identified using a statistical model containing boxcar waveforms representing each of the six experimental conditions, convolved with a canonical hemodynamic response function and mean corrected. Motion parameters defined by the realignment procedure were added to the model as six separate regressors of no interest. Multiple linear regression was then used to generate parameter estimates for each regressor at every voxel. Data were scaled to the global mean of the time series and high-pass filtered (cut-off: 0.0083 Hz) to remove low-frequency signal drifts.

To extract activity from retinotopic visual cortex, we created mask volumes for each region of interest (left and right: LGN, V1, V2d, V2v, V3d, V3v, and V5/MT, see Supplemental Data). Regression parameters resulting from analysis of the experimental imaging-time series were extracted for the maximally activated voxel (comparing visual stimulation with darkness in no-saccade conditions) in each region of interest, yielding a plot of percent-signal change for each experimental condition in LGN, V1, V2, V3, and V5/MT averaged across subjects. Averaging across all voxels in each area produced virtually identical results, confirming that the pattern of responses was consistent over each region.

To compare the effects of saccades across different brain areas, we took the mean regression parameter estimates (β) of activity in each visual condition and computed a modulation index ($\beta_{\text{no saccade}} - \beta_{\text{saccade}}$)/($\beta_{\text{no saccade}} + \beta_{\text{saccade}}$) for each subject. Modulation index values were then averaged across subjects.

Supplemental Data

Supplemental Data including Supplemental Experimental Procedures, Results, two figures, and a table are available at http://www.current-biology.com/cgi/content/full/15/1/37/DC1/.

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